

SEQUENCE LISTING

<110> Inventors: Michele A. McTigue, Steven L. Bender, Allen Borchardt, Robert S. Kania, Chris Pinko, John A. Wickersham

<120> Crystal Structure of VEGFRKD: Ligand Complexes and Methods of Use Thereof

<130> PC19173A

<140> New Filing

<141> 2004-04-[INSERT]

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<170> PatentIn version 3.1

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<212> PRT

<213> Homo sapiens

<400> 2

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35 40 45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
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Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
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Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
85 90 95

Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
100 105 110

Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
115 120 125

Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
130 135 140

Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145 150 155 160

Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
165 170 175

Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
180 185 190

Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
195 200 205

Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
210 215 220

Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225 230 235 240

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
245 250 255

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
260 265 270

Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
275 280 285

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
290 295 300

Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305 310 315 320

Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
325 330 335

Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
340 345 350

Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
355 360 365

Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
370 375 380

Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
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Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
405 410 415

Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
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Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
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Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
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Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465 470 475 480

Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
485 490 495

Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
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Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
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Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
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Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
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Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
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Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
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Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
595 600 605

Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
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Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625 630 635 640

Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
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Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
660 665 670

Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
675 680 685

Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
690 695 700

Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705 710 715 720

Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
725 730 735

Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
740 745 750

Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu
755 760 765

Val Gly Thr Ala Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile
770 775 780

Ile Leu Arg Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly
785 790 795 800

Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His
805 810 815

Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp
820 825 830

Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val
835 840 845

Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr
850 855 860

Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg
865 870 875 880

Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu
885 890 895

Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu
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Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu
915 920 925

Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg
930 935 940

Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys
945 950 955 960

Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
965 970 975

Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro
980 985 990

Glu Asp Leu Tyr Lys Asp Phe Leu Thr Leu Glu His Leu Ile Cys Tyr
995 1000 1005

Ser Phe Gln Val Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys
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Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu
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Lys Asn Val Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile
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Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly Asp Ala Arg Leu Pro
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Leu Lys Trp Met Ala Pro Glu Thr Ile Phe Asp Arg Val Tyr Thr
1070 1075 1080

Ile Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile
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Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Lys Ile Asp Glu
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Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg Met Arg Ala Pro
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Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys Trp
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His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu
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His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp Gly Lys
1160 1165 1170

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Asp Ser Gly Leu Ser Leu Pro Thr Ser Pro Val Ser Cys Met Glu
1190 1195 1200

Glu Glu Glu Val Cys Asp Pro Lys Phe His Tyr Asp Asn Thr Ala
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Gly Ile Ser Gln Tyr Leu Gln Asn Ser Lys Arg Lys Ser Arg Pro
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Val Ser Val Lys Thr Phe Glu Asp Ile Pro Leu Glu Glu Pro Glu
1235 1240 1245

Val Lys Val Ile Pro Asp Asp Asn Gln Thr Asp Ser Gly Met Val
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Leu Ala Ser Glu Glu Leu Lys Thr Leu Glu Asp Arg Thr Lys Leu
1265 1270 1275

Ser Pro Ser Phe Gly Gly Met Val Pro Ser Lys Ser Arg Glu Ser
1280 1285 1290

Val Ala Ser Glu Gly Ser Asn Gln Thr Ser Gly Tyr Gln Ser Gly
1295 1300 1305

Tyr His Ser Asp Asp Thr Asp Thr Thr Val Tyr Ser Ser Glu Glu
1310 1315 1320

Ala Glu Leu Leu Lys Leu Ile Glu Ile Gly Val Gln Thr Gly Ser
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Thr Ala Gln Ile Leu Gln Pro Asp Ser Gly Thr Thr Leu Ser Ser
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Pro Pro Val
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<212> PRT

<213> Homo sapiens

<400> 3

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Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala
35 40 45

Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met
50 55 60

Leu Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu
65 70 75 80

Leu Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu
 85 90 95

Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu
 100 105 110

Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn
 115 120 125

Glu Phe Val Pro Tyr Lys Val Ala Pro Glu Asp Leu Tyr Lys Asp Phe
 130 135 140

Leu Thr Leu Glu His Leu Ile Cys Tyr Ser Phe Gln Val Ala Lys Gly
145 150 155 160

Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu Ala Ala
 165 170 175

Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile Cys Asp Phe
 180 185 190

Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val Arg Lys Gly
 195 200 205

Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr Ile Phe Asp
 210 215 220

Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu
225 230 235 240

Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly Val Lys Ile
 245 250 255

Asp Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg Met Arg Ala
 260 265 270

Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys Trp
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His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu His
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Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp

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35 40 45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
50 55 60

Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65 70 75 80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
85 90 95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
100 105 110

Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
115 120 125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
130 135 140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145 150 155 160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
165 170 175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
180 185 190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu

195 200 205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
210 215 220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225 230 235 240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
245 250 255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
260 265 270

Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
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Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
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Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305 310 315 320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
325 330 335

Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
340 345 350

Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val

355 360 365

Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
370 375 380

Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385 390 395 400

Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
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Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
420 425 430

Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
435 440 445

Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
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Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys
465 470 475 480

Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
485 490 495

Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
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Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg

515 520 525

Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val
530 535 540

Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His
545 550 555 560

Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser
565 570 575

Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu
580 585 590

Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys
595 600 605

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Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro

675 680 685

Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu
690 695 700

Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg
705 710 715 720

Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln
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Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr Val Gln Gly Thr Ser
740 745 750

Asp Lys Ser Asn Leu Glu Leu Ile Thr Leu Thr Cys Thr Cys Val Ala
755 760 765

Ala Thr Leu Phe Trp Leu Leu Leu Thr Leu Leu Ile Arg Lys Met Lys
770 775 780

Arg Ser Ser Ser Glu Ile Lys Thr Asp Tyr Leu Ser Ile Ile Met Asp
785 790 795 800

Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro Tyr Asp
805 810 815

Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly Lys Ser
820 825 830

Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala Phe Gly

835 840 845

Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met Leu Lys
850 855 860

Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu Leu Lys
865 870 875 880

Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu Leu Gly
885 890 895

Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu Tyr Cys
900 905 910

Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp Leu Phe
915 920 925

Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys Glu Lys
930 935 940

Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp Ser Val
945 950 955 960

Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp Lys Ser
965 970 975

Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr Lys Glu
980 985 990

Pro Ile Thr Met Glu Asp Leu Ile Ser Tyr Ser Phe Gln Val Ala Arg

995 1000 1005

Gly Met Glu Phe Leu Ser Ser Arg Lys Cys Ile His Arg Asp Leu
1010 1015 1020

Ala Ala Arg Asn Ile Leu Leu Ser Glu Asn Asn Val Val Lys Ile
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Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asn Pro Asp Tyr
1040 1045 1050

Val Arg Lys Gly Asp Thr Arg Leu Pro Leu Lys Trp Met Ala Pro
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Glu Ser Ile Phe Asp Lys Ile Tyr Ser Thr Lys Ser Asp Val Trp
1070 1075 1080

Ser Tyr Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Ser
1085 1090 1095

Pro Tyr Pro Gly Val Gln Met Asp Glu Asp Phe Cys Ser Arg Leu
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Arg Glu Gly Met Arg Met Arg Ala Pro Glu Tyr Ser Thr Pro Glu
1115 1120 1125

Ile Tyr Gln Ile Met Leu Asp Cys Trp His Arg Asp Pro Lys Glu
1130 1135 1140

Arg Pro Arg Phe Ala Glu Leu Val Glu Lys Leu Gly Asp Leu Leu

1145	1150	1155
Gln Ala Asn Val Gln Gln Asp Gly Lys Asp Tyr Ile Pro Ile Asn		
1160	1165	1170
Ala Ile Leu Thr Gly Asn Ser Gly Phe Thr Tyr Ser Thr Pro Ala		
1175	1180	1185
Phe Ser Glu Asp Phe Phe Lys Glu Ser Ile Ser Ala Pro Lys Phe		
1190	1195	1200
Asn Ser Gly Ser Ser Asp Asp Val Arg Tyr Val Asn Ala Phe Lys		
1205	1210	1215
Phe Met Ser Leu Glu Arg Ile Lys Thr Phe Glu Glu Leu Leu Pro		
1220	1225	1230
Asn Ala Thr Ser Met Phe Asp Asp Tyr Gln Gly Asp Ser Ser Thr		
1235	1240	1245
Leu Leu Ala Ser Pro Met Leu Lys Arg Phe Thr Trp Thr Asp Ser		
1250	1255	1260
Lys Pro Lys Ala Ser Leu Lys Ile Asp Leu Arg Val Thr Ser Lys		
1265	1270	1275
Ser Lys Glu Ser Gly Leu Ser Asp Val Ser Arg Pro Ser Phe Cys		
1280	1285	1290
His Ser Ser Cys Gly His Val Ser Glu Gly Lys Arg Arg Phe Thr		

1295 1300 1305

Tyr Asp His Ala Glu Leu Glu Arg Lys Ile Ala Cys Cys Ser Pro
1310 1315 1320

Pro Pro Asp Tyr Asn Ser Val Val Leu Tyr Ser Thr Pro Pro Ile
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Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu
20 25 30

Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
35 40 45

Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
50 55 60

Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65 70 75 80

Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
85 90 95

Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
100 105 110

Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
115 120 125

Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
130 135 140

Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145 150 155 160

Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
165 170 175

Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
180 185 190

Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
195 200 205

Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile
210 215 220

Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225 230 235 240

Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
245 250 255

Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
260 265 270

Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His
275 280 285

Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
290 295 300

Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305 310 315 320

Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
325 330 335

Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
340 345 350

Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp
355 360 365

Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
370 375 380

Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385 390 395 400

Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
405 410 415

Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro

420

425

430

Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr

435

440

445

Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr

450

455

460

Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln

465

470

475

480

Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp

485

490

495

Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu

500

505

510

Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val

515

520

525

Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu

530

535

540

Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile

545

550

555

560

Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu

565

570

575

Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg

580

585

590

Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu

595

600

605

Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu

610

615

620

Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile

625

630

635

640

Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln

645

650

655

Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val

660

665

670

Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu

675

680

685

Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala

690

695

700

His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu

705

710

715

720

Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln

725

730

735

Arg Val Arg Glu Glu Asp Ala Gly Arg Tyr Leu Cys Ser Val Cys Asn

740 745 750

Ala Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser

755 760 765

Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val

770 775 780

Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met

785 790 795 800

Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile

805 810 815

Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser

820 825 830

Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly

835 840 845

Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala

850 855 860

Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met

865 870 875 880

Leu Lys Glu Gly Ala Thr Ala Ser Glu His Arg Ala Leu Met Ser Glu

885 890 895

Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu

900

905

910

Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu

915

920

925

Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp

930

935

940

Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe

945

950

955

960

Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser

965

970

975

Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala

980

985

990

Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Pro

995

1000

1005

Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg

1010

1015

1020

Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu

1025

1030

1035

Ala Ala Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile

1040

1045

1050

Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr
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Val Arg Lys Gly Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro
1070 1075 1080

Glu Ser Ile Phe Asp Lys Val Tyr Thr Thr Gln Ser Asp Val Trp
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Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser
1100 1105 1110

Pro Tyr Pro Gly Val Gln Ile Asn Glu Glu Phe Cys Gln Arg Leu
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Arg Asp Gly Thr Arg Met Arg Ala Pro Glu Leu Ala Thr Pro Ala
1130 1135 1140

Ile Arg Arg Ile Met Leu Asn Cys Trp Ser Gly Asp Pro Lys Ala
1145 1150 1155

Arg Pro Ala Phe Ser Glu Leu Val Glu Ile Leu Gly Asp Leu Leu
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Gln Gly Arg Gly Leu Gln Glu Glu Glu Glu Val Cys Met Ala Pro
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Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser Gln Val Ser
1190 1195 1200

Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp Ser Pro
1205 1210 1215

Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn Trp
1220 1225 1230

Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly
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Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr
1250 1255 1260

Thr Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val
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Leu Ala Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln
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Glu Ser Gly Phe Arg
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